

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**21-187**

**STATISTICAL REVIEW(S)**

## Statistical Review and Evaluation Clinical Studies

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**NDA No:** 21-187  
**Sponsor:** Organon Inc.  
**Name of Drug:** NuvaRing® (etonogestrel/ethinyl estradiol ring)  
**Indication:** Prevention of Pregnancy  
**Medical Reviewer:** Daniel Davis, M.D.  
**Statistical Reviewer:** Moh-Jee Ng  
**Date of Submission:** January 28, 2000  
**User Fee Date:** October 28, 2000

SEP 4 2000

### 1. Introduction

The sponsor has presented the results of 2 clinical studies to establish the efficacy of NuvaRing® for prevention of pregnancy. NuvaRing® combines contraceptive vaginal rings containing progestagens and estrogens. NuvaRing® has a daily in vitro release rate of 0.120 mg etonogestrel (ENG) and 0.015 mg ethinyl estradiol (EE). The studies were of 13 cycles, each cycle consisting of a 21-day ring period followed by a 7 day ring-free period. The studies required at least 10,000 cycles of exposure, and at least 200 women completing all 13 cycles. Table 1, below, summarizes these two clinical trials.

**Table 1**  
**Summary of all Clinical Trials**

Study number Start/Completed Date	# Center	Trial Design	Treatment Groups	Subjects Enrolled/Cycle of Exposures women years	# Cycles
US Studies 068003 11/97 – 6/99	48	Open-label, non-comparative, multicenter, efficacy, cycle control, safety	NuvaRing® with a declared daily release rate of 0.120 mg ENG and 0.015 mg EE vaginal	1,210/11,188 cycles 857.68	13 cycles
Non-US Studies 34219 11/97 – 6/99	53	Open-label, non-comparative, multicenter, efficacy, cycle control, safety	NuvaRing® with a declared daily release rate of 0.120 mg ENG and 0.015 mg EE vaginal	1,182/12,109 cycles 928.31	13 cycles

### 2. Clinical studies – 068003 and 34219

Study 068003 enrolled 1,210 subjects at 48 sites in the United States and Canada. Of these 1,210 subjects, 33 subjects did not use the trial medication. The remaining 1,177 subjects comprise the all-Subject-Treated Group. A total of 482 of the 1,177 treated subjects discontinued from the trial.

Study 34219 enrolled 1,182 subjects at 53 sites in 12 different European countries. Of these 1,182 subjects, 37 subjects did not use trial medication. The remaining 1,145 subjects comprise the all-subject-treated group. 806 subjects completed the study.

### **3. Sponsor's Contraceptive Efficacy Method**

The primary efficacy parameter was contraceptive effectiveness; the secondary efficacy parameter was cycle control. The intent-to-treat (ITT) group consisted of subjects who received at least one ring. The Per Protocol (PP) group consisted of all subjects from the ITT group without any major protocol violation. Contraceptive effectiveness was based on the occurrence of pregnancy in the ITT and PP with a 95% confidence interval. The emphasis was on the ITT group. Pregnancy risk was estimated by the Pearl Index. The Pearl Index is defined as the number of in-treatment pregnancies times 1300 divided by the total number of cycles of exposure.

- Pre-Treatment pregnancies – those in which conception occurred prior to intake of study drug: 15 in study 68003 and 10 in study 34219
- In-treatment pregnancies – those in which conception occurred after the first ring was taken and prior to discontinuation of the study drug: 15 in 068003 and 6 in 34219.
- Post-treatment pregnancies – those in which conception occurred after discontinuation of study drug: 12 in 068003 and 15 in 34219.

### **4. Results of Sponsor's and Reviewer's Contraceptive Efficacy Analysis**

This reviewer's analyses are based on the ITT evaluation groups from the sponsor's data sets. This reviewer confirmed the Pearl Index obtained by the sponsor. However, the FDA medical reviewer would like to reclassify subject 4321 of study 068003 as an in-treatment pregnancy instead of the post-pregnancy defined by the sponsor (see details in the medical review). This increases the number of in-treatment pregnancies from 15 to 16 for study 068003 and the Pearl Index estimate is 1.859 (95% CI: 1.067, 3.009). For the combined study (studies 68003 and 343219) the in-treatment pregnancies increase from 21 to 22 and the Pearl Index is estimated to be 1.238 (.726, 1.852).

The FDA medical reviewer also would like to count subjects 1934, 4820, and 4321 of study 068003 and 0524 of study 34219 as PP pregnancies (see details in the medical review). For study 068003 the number of in-treatment pregnancies increases from 5 to 8 and the Pearl Index is estimated to be 1.452 (95% CI: .631, 2.855). For study 34219 the number of in-treatment pregnancies increases from 3 to 4 and the Pearl Index is estimated to be .526 (95% CI: 0.138, 1.338).

The sponsor later submitted additional contraception efficacy results by age < 35 and ≥ 35 (June 9, 2000). The efficacy results from the sponsor and this reviewer are summarized in Tables 2 and 3 below.

**Table 2**  
**Efficacy Analyses**  
**Intent-to-Treat Evaluation Groups**

		068003		34219		Combined Studies	
<b>Sponsor's Result</b>	<b>Total # of subjects</b>	1,177		1,145		2,322	
	<b>28-day cycles</b>	11,188.1		12,109.4		23,297.6	
	<b>Woman years</b>	857.7		928.3		1,786	
	<b>In-treatment pregnancies</b>	15		6		21	
	<b>Pearl index with 95% CI</b>	1.749 (0.979,2.885)		0.646 (0.237,1.407)		1.176 (0.728; 1.797)	
<b>Reviewer's Result</b>	<b>In-treatment pregnancies</b>			6			
	<b>Pearl index with 95% CI</b>			0.646 (0.237,1.407)			
		<b>&lt; 35years</b>	<b>≥35 years</b>	<b>&lt; 35years</b>	<b>≥35 years</b>	<b>&lt; 35years</b>	<b>≥35 years</b>
<b>Sponsor's Result</b>	<b>Total # of subjects</b>	963	214	957	188	1920	402
	<b>28-day cycles</b>	9024	2164.1	10029.3	2080	19053.4	4244.2
	<b>Woman years</b>	694	165.9	771.5	159.5	1460.6	325.4
	<b>In-treatment pregnancies</b>	13	2	5	1	18	3
	<b>Pearl index with 95% CI</b>	1.873 (1.001,3.190)	1.206 (.146,4.355)	.648 (.211,1.528)	.627 (.016,3.490)	1.232 (.734,1.939)	.922 (.185,2.695)
<b>Reviewer's Result</b>	<b>In-treatment pregnancies</b>		2	5	1		3
	<b>Pearl index with 95% CI</b>		1.206 (.146,4.355)	.648 (.211,1.528)	.627 (.016,3.490)		.922 (.185,2.695)

The gray cells represent this reviewer's results that differ from the sponsor's results.

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ON ORIGINAL**

**Table 3**  
**Efficacy Analyses**  
**Per Protocol Evaluation Groups**

		068003		34219		Combined Studies	
<b>Sponsor's Result</b>	<b>Total # of subjects</b>	966		1,049		2,015	
	<b>28-day cycles</b>	7,169.4		9,879.6		17,049	
	<b>Woman years</b>	549.6		757.4		1,311	
	<b>In-treatment pregnancies</b>	5		3		8	
	<b>Pearl index with 95 % CI</b>	0.906 (0.295,2.123)		0.396 (0.082,1.158)		0.617 (0.266,1.216)	
<b>Reviewer's Result</b>	<b>In-treatment pregnancies</b>						
	<b>Pearl index with 95 % CI</b>						
		< 35years	≥35 years	< 35years	≥35 years	< 35years	≥35 years
<b>Sponsor's Result</b>	<b>Total # of subjects</b>	788	178	881	168	1669	346
	<b>28-day cycles</b>	5640.4	1392.1	8150.1	1729.5	13790.4	3121.6
	<b>Woman years</b>	432.4	106.7	624.8	132.6	1057.2	239.3
	<b>In-treatment pregnancies</b>	4	1	3	0	7	1
	<b>Pearl index with 95 % CI</b>	.925 (.252,2.369)	.937 (.024,5.221)	.479 (.099,1.403)	0	.662 (.266,1.360)	.418 (.011,2.328)
<b>Reviewer's Result</b>	<b>In-treatment pregnancies</b>		1		0		1
	<b>Pearl index with 95 % CI</b>		.937 (.024,5.221)		0		.418 (.011,2.328)

The gray cells represent this reviewer's results that differ from the sponsor's results.

**APPEARS THIS WAY  
ON ORIGINAL**

## 5. Reviewer's Comments

This reviewer's results for the Pearl Index are consistent with those of the sponsor's for both studies individually and for the combined studies. At the request of the medical reviewer, 1 post-treatment pregnancy was reclassified as an in-treatment pregnancy for the ITT evaluation group. With this additional pregnancy, the Pearl Indices increase from 1.749 to 1.859 for study 068003, and 1.176 to 1.238 for the combined studies. For age less than thirty-five years old, the Pearl Indices increase from 1.873 to 2.017 for study 068003, and 1.232 to 1.296 for the combined studies. Because the pregnancy is for a woman less than thirty-five years old, the Pearl Index for women greater than thirty-five is not affected.

The medical reviewer added 4 pregnancies to the per protocol pregnancies. Therefore, the Pearl indices increase from 0.906 to 1.452 for study 068003, 0.396 to 0.526 for study 34219, and 0.617 to 0.915 for the combined studies. For age less than thirty-five years old, the Pearl Indices increase from 0.925 to 1.613 for study 068003, 0.479 to .638 for study 34219, and .662 to 1.037 for the combined studies.

*/S/* *9/29/00*  
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Mathematical Statistician

Concur: Lisa Kammerman, Ph.D.

*/S/*  
*9/29/00*

Ed Nevius, Ph.D.

*/S/* *10/4/00*

cc. Original NDA 21-187  
HFD-580 / Division file  
HFD-580 / Daniel Davis, M.D.  
HFD-580 / Jennifer Mercier, B.S.  
HFD-715/ENevius,LKammerman, MNg

**Statistical Review and Evaluation**  
(Carcinogenicity)

Date: OCT 10 2000

**NDA No.:** 21-187

**Applicant:** Organon Inc.

**Name of Drug:** NuvaRing® (etonogestrel/ethinyl estradiol ring)

**Documents Reviewed:** A 24 month Oncogenicity Study of Org 3236 in the Rat via Subcutaneous Implants, [REDACTED] Study No. 92-2195, dated July 11, 1996.

A CDROM containing the one-year histopathology electronic data sets.

**Reviewing Pharmacologist:** Krishan L. Raheja, Ph.D., HFD-580

**Statistical Reviewer:** Karl K. Lin, Ph.D., HFD-715

**Summary of Review**

The sponsor did not perform any statistical analysis on the histopathological data. The results of this review are based on the reviewer's analysis.

Results of the analysis of the mortality data of male rats show that the dose-response trend in mortality is statistically significant, and that the survival distributions of the treatment groups are statistically significant. There is no statistically significant positive trend in incidence rate detected in the tumor types tested in male rats.

The dose-response trend in mortality in data of female rats is statistically significant. The survival distributions of the treatment groups are also statistically significant. There is no statistically significant positive trend in incidence rate detected in the tumor types tested except benign broncho/alveolar adenoma in the lungs in female rats.

**I. Introduction**

The carcinogenicity study was conducted only on rats. The purpose of the study was to evaluate the carcinogenic potential of the drug administered by subcutaneous implants to the animals for two years. The electronic data sets submitted by the sponsor are used in the reviewer's analysis.

Dr. Raheja of HFD-580 requested the Division of Biometrics 2 to conduct a statistical review of this study.

## **II. Study Design**

152 male and 201 female Sprague-Dawley rats were used in this carcinogenicity experiment. The treatment groups and numbers of animals in the groups in the experiment are presented as follows:

Group	Test Substance	Dose Level ( $\mu\text{g/day}$ Org 3236)	Number of Animals	
			Male	Female
I	Implant EVA covered with a silastic layer	0	52	51
II	Implant EVA covered with a silastic layer and adhered with Ethyl Loctite	0	0	50
III	Implant releasing Org 3236	10	50	50
IV	Implant releasing Org 3236	20	50	50

## **III. Reviewer's Analysis, Results**

The survival data were analyzed using the generalized Kruskal-Wallis method of Gehan and Breslow and Wilcoxon, and the method of Cox to test trend and homogeneity in survival. The Kruskal-Wallis method places greater weight on early deaths than does the Cox method that assigns equal weights to all death.

The prevalence method, the death-rate method, and the onset-rate method were used to test the significance of positive trend in incidence of tumor types observed under the incidental, fatal, and mortality-independent contexts, respectively. The above methods adjust for differences in mortality among different treatment groups. Since only one species was used in this study, the positive trend in incidence rate is tested at 0.05 for rare tumor types, and 0.01 for common tumor types. A tumor type is classified as rare if its spontaneous rate is 1% or less, and as common, otherwise. When the above decision rule is followed in the tumor data analysis, the overall false positive rate is about 10%.

### **III.1 Male Rats**

The mortality data of male rats presented in Tables 1 and 2, and Figures 1 and 2. Results of the analysis of the mortality data of male rats show that the dose-response trend in mortality is statistically significant, and that the survival distributions of the treatment groups are statistically significant in both the Cox test and the Kruskal-Wallis test. The p-values for the Cox test are  $p=0.0164$  for the trend test and 0.0237 for the homogeneity test. The p-values for the Kruskal-



Wallis test are  $p=0.0055$  for the trend test and 0.0108 for the homogeneity test. The results of the analysis of mortality data of male rats are presented in Table 3.

There is no statistically significant positive trend in incidence rate detected in the tumor types tested in male rats. The results of the tests for positive trend in tumor incidence are presented in Table 4.

### III.2 Female Rats

The mortality data of female rats presented in Tables 5 and 6, and Figures 3 and 4. The dose-response trend in mortality in female rats data is also statistically significant in either the Cox test ( $p=0.0296$ ) or the Kruskal-Wallis test ( $p=0.0086$ ). The test of homogeneity of survival distributions of the treatment groups is not statistically significant in the Cox test (0.0527), but is statistically significant in the Kruskal-Wallis test (0.0248). The results of the analysis of mortality data of female rats are presented in Table 7.

There is no statistically significant positive trend in incidence rate detected in the tumor types tested except benign broncho/alveolar adenoma in the lungs in female rats ( $p=0.042$ ). The tumor incidence rates are as follows:

Organ	Tumor type	Control 1	Control 2	Medium	High	p-value
Lungs	Benign broncho/alveolar adenoma	0/51	0/50	0/50	2/50	0.042

The results of the tests for positive trend in tumor incidence are presented in Table 8.

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Karl K. Lin, Ph.D.  
Expert Mathematical Statistician  
(Applications in Pharmacology and Toxicology)

/S/

Concur: S. Edward Nevius, Ph.D.  
Director, Division of Biometrics II

cc: Original/NDA 21-187 File  
HFD-580/K Rajaja, A Jordan  
HFD-715/Chron  
HFD-715/E Nevius, K Lin

Figure 1

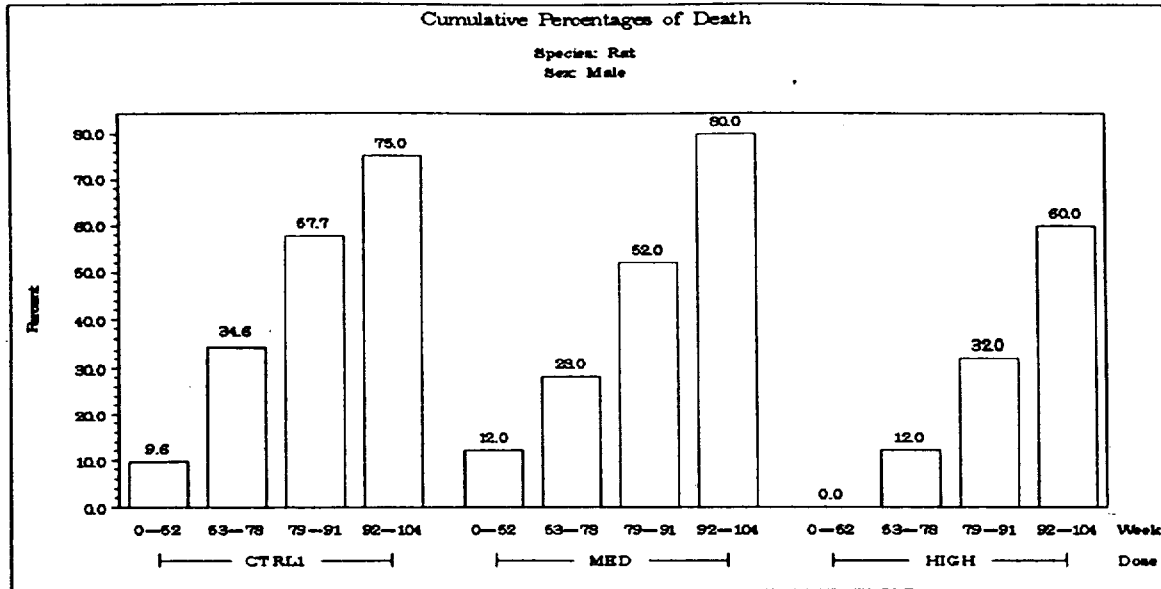


Figure 2

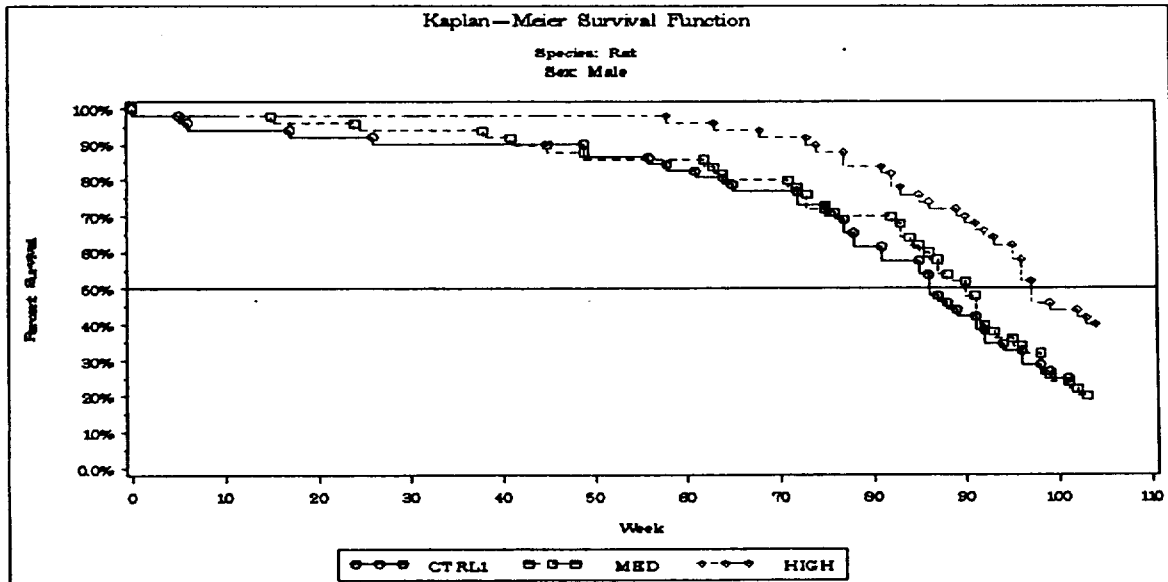


Table 1

Number of Animals  
Species: Rat  
Sex: Male

Week	Treatment Group			
	CTRL1	MED	HIGH	Total
	N	N	N	N
0-52	5	6	.	11
53-78	13	8	6	27
79-91	12	12	10	34
92-104	9	14	14	37
105-105	13	10	20	43
Total	52	50	50	152

Source: C:\NEVIUS\XAnimalX.txt

Table 2

Analysis of Mortality  
Species: Rat  
Sex: Male

Week	Dose								
	CTRL1			MED			HIGH		
	NUM. of Dead	NUM. at Risk	CUMU Pct. Died	NUM. of Dead	NUM. at Risk	CUMU Pct. Died	NUM. of Dead	NUM. at Risk	CUMU Pct. Died
0-52	5	52	9.6	6	50	12.0	.	.	.
53-78	13	47	34.6	8	44	28.0	6	50	12.0
79-91	12	34	57.7	12	36	52.0	10	44	32.0
92-104	9	22	75.0	14	24	80.0	14	34	60.0
105-105	13	52	25.0	10	50	20.0	20	50	40.0

Table 3

Dose-Mortality Trend Tests

This test is run using Trend and Homogeneity Analyses of Proportions and Life Table Data Version 2.1, by Donald G. Thomas, National Cancer Institute

Species: Rat  
Sex: Male

Method	Time-Adjusted Trend Test	Statistic	P Value
Cox	Dose-Mortality Trend	5.76	0.0164
	Depart from Trend	1.73	0.1885
	Homogeneity	7.49	0.0237
Kruskal-Wallis	Dose-Mortality Trend	7.72	0.0055
	Depart from Trend	1.34	0.2468
	Homogeneity	9.06	0.0108

Source: C:\NEVIUS\XAnimals\X.txt

Table 4

Analysis of Carcinogenic Potential in Male Rat  
 Test of Dose-Response (Tumor) Positive Linear Trend  
 Study No. STUDY4412

Source:  

Note: Dose Levels Included: CTRL1 MED HIGH (0 10 20)  
 Missing value in Tumor-Caused Death is treated as tumor not causing death  
 Tumor Type: IN: Incidental (nonfatal) tumor, FA: Fatal tumor.

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
ADRENAL GLANDS	(AD	) IN 92-104	1	1 1 0	0.762 0.679 0.688
U/ MED: MALIGNANT NEO	(141	) IN 92-104	2	8 13 14	
		IN 105-105	1	1 1 2	
		IN 105-105	2	12 9 18	
Spontaneous tumor pct: 4%	in ctrl.	- Total	-	2 2 2	
ADRENAL GLANDS	(AD	) IN 53-78	1	0 1 0	0.548 0.481 0.487
U/ MED: BENIGN NEO	(142	) IN 53-78	2	13 7 6	
		IN 79-91	1	3 1 1	
		IN 79-91	2	9 11 9	
		IN 92-104	1	1 0 1	
		IN 92-104	2	8 14 13	
		IN 105-105	1	1 2 4	
		IN 105-105	2	12 8 16	
Spontaneous tumor pct: 10%	in ctrl.	- Total	-	5 4 6	
ADRENAL GLANDS	(AD	) IN 105-105	1	1 0 1	0.769 0.606 0.622
U/ CTX: CARCINOMA	(188	) IN 105-105	2	12 10 19	
Spontaneous tumor pct: 2%	in ctrl.	- Total	-	1 0 1	
ADRENAL GLANDS	(AD	) IN 79-91	1	1 1 1	0.963 0.942 0.945
B/ MED: BENIGN NEOPLASM	(274	) IN 79-91	2	11 11 9	
		IN 92-104	1	2 2 0	
		IN 92-104	2	7 12 14	
		IN 105-105	1	1 1 0	
		IN 105-105	2	12 9 20	
Spontaneous tumor pct: 8%	in ctrl.	- Total	-	4 4 1	
ADRENAL GLANDS	(AD	) IN 53-78	1	1 0 0	0.748 0.658 0.668
U/ CTX: ADENOMA	(395	) IN 53-78	2	12 8 6	
		IN 79-91	1	1 1 1	
		IN 79-91	2	11 11 9	
		IN 105-105	1	0 1 0	
		IN 105-105	2	13 9 20	
Spontaneous tumor pct: 4%	in ctrl.	- Total	-	2 2 1	
ADRENAL GLANDS	(AD	) IN 92-104	1	0 1 0	0.756 0.569 0.594
B/ MED: MALIGNANT NEO	(603	) IN 92-104	2	9 13 14	
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	0 1 0	

Table 4 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2x2 CONTINGENCY -----TABLES-----			EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)		
STERNAL MARROW	(BM1	) IN 0-52	1	0	1	0	0.500	0.158	0.184
TISSUE MISSING	(000	) IN 0-52	2	5	4	0			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	0			
FEMORAL MARROW	(BM2	) IN 79-91	1	0	0	1	0.272	0.084	0.094
TISSUE MISSING	(000	) IN 79-91	2	12	12	8			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	1			
BRAIN	(BN	) IN 105-105	1	0	1	0	0.908	0.851	0.861
MALIGNANT GLIOMA	(458	) IN 105-105	2	13	9	20			
		FA 86	1	1	0	0			
		FA 86	2	29	31	38			
Spontaneous tumor pct: 2% in ctrl. - Total			-	1	1	0			
BRAIN	(BN	) FA 56	1	1	0	0	1.000	0.891	0.901
HEMANGIOSARCOMA	(463	) FA 56	2	46	44	50			
Spontaneous tumor pct: 2% in ctrl. - Total			-	1	0	0			
BRAIN	(BN	) FA 92	1	0	1	0	0.725	0.572	0.596
GRANULAR C-TUMOR	(589	) FA 92	2	22	23	34			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	0			
BONE	(BO	) IN 79-91	1	0	0	1	0.272	0.084	0.094
TISSUE MISSING	(000	) IN 79-91	2	12	12	8			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	1			
STERNUM	(BO1	) IN 0-52	1	0	1	0	0.500	0.158	0.184
TISSUE MISSING	(000	) IN 0-52	2	5	4	0			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	0			
FEMUR	(BO2	) IN 79-91	1	0	0	1	0.272	0.084	0.094
TISSUE MISSING	(000	) IN 79-91	2	12	12	8			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	1			
CECUM	(CE	) IN 53-78	1	1	1	0	0.297	0.223	0.230
TISSUE MISSING	(000	) IN 53-78	2	11	6	6			
		IN 79-91	1	1	1	2			
		IN 79-91	2	10	10	6			
		IN 92-104	1	0	1	1			
		IN 92-104	2	9	12	12			
Spontaneous tumor pct: 4% in ctrl. - Total			-	2	3	3			

Table 4 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2x2 CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
COLON	(CO	) IN 53-78	1	1 0 0	0.559 0.437 0.450
TISSUE MISSING	(000	) IN 53-78	2	11 8 6	
		IN 79-91	1	1 0 1	
		IN 79-91	2	10 12 8	
		IN 92-104	1	0 0 1	
		IN 92-104	2	9 14 12	
Spontaneous tumor pct: 4%		in ctrl. - Total	-	2 0 2	
DUODENUM	(DU	) IN 53-78	1	0 1 0	0.352 0.252 0.261
TISSUE MISSING	(000	) IN 53-78	2	13 6 6	
		IN 79-91	1	1 0 1	
		IN 79-91	2	10 12 8	
		IN 92-104	1	0 1 1	
		IN 92-104	2	9 12 12	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	1 2 2	
EPIDIDYMIDES	(EP	) IN 79-91	1	0 0 1	0.272 0.084 0.094
TISSUE MISSING	(000	) IN 79-91	2	12 12 8	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 0 1	
ESOPHAGUS	(ES	) IN 79-91	1	0 0 1	0.272 0.084 0.094
TISSUE MISSING	(000	) IN 79-91	2	12 12 8	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 0 1	
EXTREMITY	(EX	) IN 92-104	1	1 0 0	0.931 0.875 0.883
TISSUE MISSING	(000	) IN 92-104	2	7 14 14	
		IN 105-105	1	0 1 0	
		IN 105-105	2	13 8 20	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	1 1 0	
EYES	(EY	) IN 0-52	1	0 1 0	0.244 0.145 0.153
TISSUE MISSING	(000	) IN 0-52	2	5 4 0	
		IN 79-91	1	1 0 1	
		IN 79-91	2	10 12 8	
		IN 92-104	1	0 0 1	
		IN 92-104	2	9 14 12	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	1 1 2	
EYES	(EY	) IN 92-104	1	1 0 0	1.000 0.924 0.933
U/ AMELANOTIC MELANOMA	(314	) IN 92-104	2	8 14 13	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	1 0 0	
HARDERIAN GLAND	(HG	) IN 105-105	1	1 0 0	1.000 0.911 0.920
ADENOMA	(172	) IN 105-105	2	12 10 20	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	1 0 0	

Table 4 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
ILEUM	(IL	) IN 53-78	1	1 1 0	0.114 0.073 0.076
TISSUE MISSING	(000	) IN 53-78	2	11 6 6	
		IN 79-91	1	1 1 3	
		IN 79-91	2	10 10 4	
		IN 92-104	1	0 0 1	
		IN 92-104	2	9 14 12	
Spontaneous tumor pct: 4%		in ctrl. - Total	-	2 2 4	
JEJUNUM	(JE	) IN 0-52	1	2 1 0	0.129 0.098 0.100
TISSUE MISSING	(000	) IN 0-52	2	1 4 0	
		IN 53-78	1	4 2 3	
		IN 53-78	2	5 4 0	
		IN 79-91	1	5 0 6	
		IN 79-91	2	2 12 -2	
		IN 92-104	1	1 2 3	
		IN 92-104	2	7 10 8	
Spontaneous tumor pct: 23%		in ctrl. - Total	-	12 5 12	
JEJUNUM	(JE	) IN 105-105	1	1 0 0	1.000 0.911 0.920
CARCINOMA	(279	) IN 105-105	2	12 10 20	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	1 0 0	
KIDNEYS	(KD	) IN 105-105	1	1 0 0	1.000 0.911 0.920
U/ MALIG MESENCHYMAL TUMO	(261	) IN 105-105	2	12 10 20	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	1 0 0	
KIDNEYS	(KD	) IN 53-78	1	1 0 0	1.000 0.823 0.839
U/ CTX: TUB ADENOMA	(614	) IN 53-78	2	12 8 6	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	1 0 0	
MESENTERIC LN	(L1	) IN 79-91	1	0 1 1	0.350 0.221 0.232
TISSUE MISSING	(000	) IN 79-91	2	12 10 8	
		IN 92-104	1	0 1 0	
		IN 92-104	2	9 12 14	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 2 1	
MESENTERIC LN	(L1	) IN 79-91	1	0 1 0	0.625 0.453 0.478
HEMANGIOSARCOMA	(682	) IN 79-91	2	12 10 9	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 1 0	
MEDIASTINAL LN	(L2	) IN 0-52	1	0 1 0	0.771 0.684 0.693
TISSUE MISSING	(000	) IN 0-52	2	5 4 0	
		IN 79-91	1	1 1 0	
		IN 79-91	2	10 10 10	
		IN 92-104	1	0 3 0	
		IN 92-104	2	9 8 14	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	1 5 0	



Table 4 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2x2 CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
MEDIASTINAL LN	(L2	) IN 53-78	1	0 1 0	0.518 0.372 0.396
HEMANGIOSARCOMA	(684	) IN 53-78	2	13 7 6	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 1 0	
LACRIMAL GLANDS	(LG	) IN 53-78	1	0 1 0	0.549 0.461 0.470
TISSUE MISSING	(000	) IN 53-78	2	13 6 6	
		IN 79-91	1	1 4 0	
		IN 79-91	2	10 4 10	
		IN 92-104	1	0 1 1	
		IN 92-104	2	9 12 12	
Spontaneous tumor pct: 2% in ctrl. - Total			-	1 6 1	
LIVER	(LI	) IN 105-105	1	1 1 0	0.913 0.864 0.873
HEPATO: CARCINOMA	(260	) IN 105-105	2	12 9 20	
Spontaneous tumor pct: 2% in ctrl. - Total			-	1 1 0	
LIVER	(LI	) IN 79-91	1	0 1 0	0.647 0.470 0.495
HEPATOCELLULAR ADENOMA	(672	) IN 79-91	2	12 11 10	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 1 0	
LYMPH/RETIC TIS	(LR	) FA 82	1	0 0 1	0.381 0.132 0.146
HISTIOCYTIC SARCOMA	(221	) FA 82	2	32 36 41	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 0 1	
LYMPH/RETIC TIS	(LR	) FA 75	1	1 0 0	1.000 0.969 0.972
MYELOSARC/GRAN-LEUK	(315	) FA 75	2	39 38 45	
		FA 92	1	1 0 0	
		FA 92	2	21 24 34	
Spontaneous tumor pct: 4% in ctrl. - Total			-	2 0 0	
LYMPH/RETIC TIS	(LR	) FA 92	1	0 0 1	0.425 0.150 0.165
MALIGNANT LYMPHOMA	(497	) FA 92	2	22 24 33	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 0 1	
LUNGS	(LU	) IN 79-91	1	0 1 0	0.369 0.223 0.236
BRNCH-ALVEO CARCINOMA	(281	) IN 79-91	2	12 11 10	
		IN 105-105	1	0 0 1	
		IN 105-105	2	13 10 19	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 1 1	
LUNGS	(LU	) IN 105-105	1	0 0 1	0.465 0.165 0.180
BRONCHO/ALVEOLAR ADENOMA	(371	) IN 105-105	2	13 10 19	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 0 1	

Table 4 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
MAMMARY	(MG	) IN 0-52	1	1 1 0	0.986 0.981 0.982
TISSUE MISSING	(000	) IN 0-52	2	3 4 0	
		IN 53-78	1	9 4 1	
		IN 53-78	2	-5 0 4	
		IN 79-91	1	5 5 2	
		IN 79-91	2	2 2 6	
		IN 92-104	1	3 3 4	
		IN 92-104	2	3 8 6	
		IN 105-105	1	2 2 4	
		IN 105-105	2	9 6 12	
Spontaneous tumor pct: 38% in ctrl. - Total				-	20 15 11
MAMMARY	(MG	) IN 92-104	1	0 1 1	0.441 0.250 0.266
FIBROADENOMA	(082	) IN 92-104	2	6 10 9	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 1 1
MESEN/PERITONEUM	(MS	) IN 92-104	1	1 0 0	1.000 0.928 0.936
LIPOSARCOMA	(613	) IN 92-104	2	8 14 14	
Spontaneous tumor pct: 2% in ctrl. - Total				-	1 0 0
OPTIC NERVE	(ON	) IN 79-91	1	0 1 1	0.126 0.063 0.068
TISSUE MISSING	(000	) IN 79-91	2	12 10 8	
		IN 92-104	1	0 0 1	
		IN 92-104	2	9 14 12	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 1 2
PANCREAS	(PA	) IN 53-78	1	0 1 0	0.309 0.206 0.215
TISSUE MISSING	(000	) IN 53-78	2	13 6 6	
		IN 79-91	1	1 0 1	
		IN 79-91	2	10 12 8	
		IN 92-104	1	0 0 1	
		IN 92-104	2	9 14 12	
Spontaneous tumor pct: 2% in ctrl. - Total				-	1 1 2
PANCREAS	(PA	) IN 79-91	1	0 1 0	0.133 0.080 0.085
ISLET C: ADENOMA	(384	) IN 79-91	2	11 11 9	
		IN 92-104	1	0 1 1	
		IN 92-104	2	9 13 12	
		IN 105-105	1	0 0 2	
		IN 105-105	2	13 10 18	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 2 3
PANCREAS	(PA	) IN 79-91	1	0 0 1	0.101 0.038 0.042
ACINAR C: ADENOMA	(432	) IN 79-91	2	11 12 8	
		IN 92-104	1	0 0 1	
		IN 92-104	2	9 14 12	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 0 2

Table 4 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
PITUITARY GLAND	(PG	) IN 92-104	1	0 1 0	0.750 0.570 0.594
TISSUE MISSING	(000	) IN 92-104	2	9 12 14	
Spontaneous tumor pct: <= 1% in ctrl. - Total				0 1 0	
PITUITARY GLAND	(PG	) IN 53-78	1	4 4 0	0.432 0.399 0.402
P-DIST: ADENOMA	(083	) IN 53-78	2	8 4 5	
		IN 79-91	1	1 2 6	
		IN 79-91	2	4 5 2	
		IN 92-104	1	3 2 5	
		IN 92-104	2	5 7 6	
		IN 105-105	1	5 7 14	
		IN 105-105	2	8 3 6	
		FA 74	1	0 0 1	
		FA 74	2	40 37 45	
		FA 78	1	1 0 0	
		FA 78	2	35 35 44	
		FA 81	1	2 0 0	
		FA 81	2	32 35 44	
		FA 82	1	0 1 0	
		FA 82	2	32 34 42	
		FA 83	1	0 0 1	
		FA 83	2	32 34 40	
		FA 84	1	0 1 0	
		FA 84	2	32 32 39	
		FA 85	1	1 0 0	
		FA 85	2	31 31 39	
		FA 86	1	0 1 1	
		FA 86	2	30 29 37	
		FA 87	1	1 0 0	
		FA 87	2	27 29 37	
		FA 88	1	1 2 0	
		FA 88	2	24 26 37	
		FA 89	1	1 0 0	
		FA 89	2	23 26 37	
		FA 91	1	1 0 0	
		FA 91	2	22 25 35	
		FA 92	1	0 1 0	
		FA 92	2	22 22 34	
		FA 96	1	0 0 1	
		FA 96	2	18 18 30	
		FA 99	1	0 2 1	
		FA 99	2	15 14 25	
		FA 101	1	1 0 0	
		FA 101	2	13 13 23	
		FA 102	1	0 1 0	
		FA 102	2	13 11 23	
		FA 103	1	0 0 1	
		FA 103	2	13 11 21	
Spontaneous tumor pct: 42% in ctrl. - Total				22 24 31	

Table 4 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
PITUITARY GLAND	(PG	) IN 105-105	1	0 1 0	0.777 0.620 0.636
P-DIST: CARCINOMA	(581	) IN 105-105	2	13 9 20	
		FA 95	1	0 1 0	
		FA 95	2	18 18 32	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 2 0	
PARATHYROID GLS.	(PT	) IN 53-78	1	0 1 1	0.352 0.290 0.296
TISSUE MISSING	(000	) IN 53-78	2	13 6 4	
		IN 79-91	1	1 2 3	
		IN 79-91	2	10 8 4	
		IN 92-104	1	0 0 1	
		IN 92-104	2	9 14 12	
		IN 105-105	1	4 1 2	
		IN 105-105	2	5 8 16	
Spontaneous tumor pct: 10% in ctrl. - Total			-	5 4 7	
PARATHYROID GLS.	(PT	) IN 92-104	1	1 0 0	1.000 0.924 0.933
ADENOMA	(554	) IN 92-104	2	8 14 13	
Spontaneous tumor pct: 2% in ctrl. - Total			-	1 0 0	
LOW COLON/RECTUM	(RC	) IN 53-78	1	1 0 0	0.559 0.437 0.450
TISSUE MISSING	(000	) IN 53-78	2	11 8 6	
		IN 79-91	1	1 0 1	
		IN 79-91	2	10 12 8	
		IN 92-104	1	0 0 1	
		IN 92-104	2	9 14 12	
Spontaneous tumor pct: 4% in ctrl. - Total			-	2 0 2	
CERVICAL SC	(SC1	) IN 92-104	1	1 0 0	1.000 0.936 0.944
TISSUE MISSING	(000	) IN 92-104	2	7 14 14	
Spontaneous tumor pct: 2% in ctrl. - Total			-	1 0 0	
SKIN	(SK	) IN 79-91	1	1 0 0	1.000 0.888 0.899
TISSUE MISSING	(000	) IN 79-91	2	10 12 10	
Spontaneous tumor pct: 2% in ctrl. - Total			-	1 0 0	
SKIN	(SK	) IN 79-91	1	0 0 2	0.085 0.031 0.035
MYXOSARCOMA	(358	) IN 79-91	2	11 12 8	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 0 2	
SKIN	(SK	) IN 105-105	1	0 0 1	0.465 0.165 0.180
PILOMATRIXOMA	(373	) IN 105-105	2	13 10 19	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 0 1	
SKIN	(SK	) IN 92-104	1	1 1 0	0.746 0.622 0.636
FIBROSARCOMA	(381	) IN 92-104	2	8 13 14	
		IN 105-105	1	0 0 1	
		IN 105-105	2	13 10 19	
Spontaneous tumor pct: 2% in ctrl. - Total			-	1 1 1	

Table 4 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2x2 CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
SKIN	(SK	) IN 92-104	1	1 0 2	0.343 0.237 0.246
FIBROMA	(385	) IN 92-104	2	8 14 12	
		IN 105-105	1	0 1 1	
		IN 105-105	2	13 9 19	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	1 1 3	
SKIN	(SK	) IN 79-91	1	1 0 0	0.899 0.832 0.843
LIPOMA	(396	) IN 79-91	2	10 12 10	
		IN 105-105	1	0 1 0	
		IN 105-105	2	13 9 20	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	1 1 0	
SKIN	(SK	) IN 79-91	1	0 1 0	0.704 0.537 0.555
BASAL CELL CARCINOMA	(675	) IN 79-91	2	11 11 10	
		IN 92-104	1	0 1 0	
		IN 92-104	2	9 13 14	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 2 0	
IMPLANT ST-COMB	(SK3	) IN 79-91	1	0 1 0	0.026 0.017 0.018
ZT: CAPSULE-IMPLANT SITE	(050	) IN 79-91	2	12 10 10	
		IN 92-104	1	0 1 0	
		IN 92-104	2	9 12 14	
		IN 105-105	1	3 5 9	
		IN 105-105	2	7 0 2	
Spontaneous tumor pct: 6%		in ctrl. - Total	-	3 7 9	
IMPLANT ST-COMB	(SK3	) IN 105-105	1	0 1 0	0.615 0.517 0.539
FIBROMA	(744	) IN 105-105	2	10 4 11	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 1 0	
SPLEEN	(SP	) IN 79-91	1	0 0 1	0.272 0.084 0.094
TISSUE MISSING	(000	) IN 79-91	2	12 12 8	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 0 1	
SPLEEN	(SP	) IN 92-104	1	0 1 0	0.756 0.569 0.594
LEIOMYOSARCOMA	(608	) IN 92-104	2	9 13 14	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 1 0	
STOMACH	(ST	) IN 92-104	1	0 0 1	0.361 0.125 0.139
TISSUE MISSING	(000	) IN 92-104	2	9 14 12	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 0 1	
TAIL	(TA	) IN 79-91	1	1 0 0	0.400 0.260 0.272
TISSUE MISSING	(000	) IN 79-91	2	10 12 10	
		IN 92-104	1	0 0 2	
		IN 92-104	2	9 14 10	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	1 0 2	

Table 4 (continued)

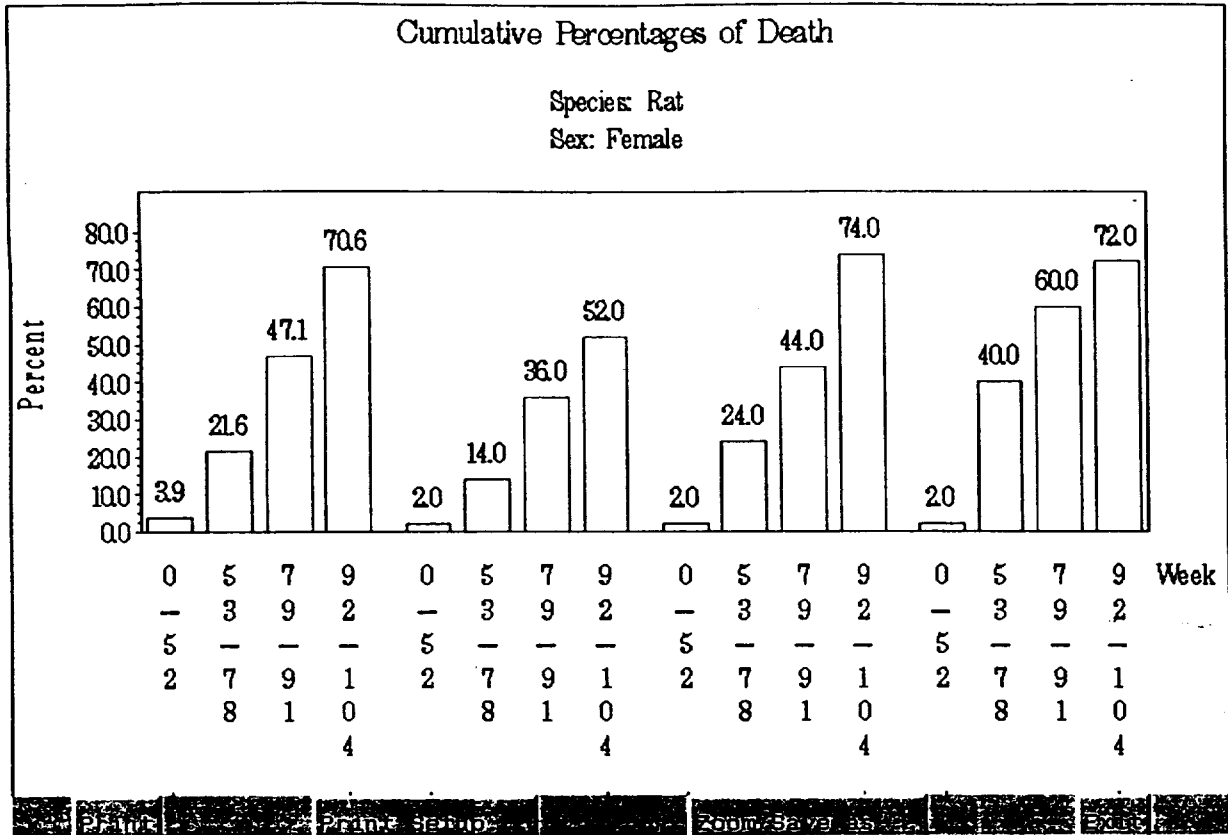
ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
TESTES	(TE )	IN 79-91	1	0 0 1	0.272 0.084 0.094
TISSUE MISSING	(000 )	IN 79-91	2	12 12 8	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 0 1	
TESTES	(TE )	IN 79-91	1	1 0 0	0.960 0.926 0.930
U/ INTERSTIT C-TUMOR	(138 )	IN 79-91	2	11 12 9	
		IN 92-104	1	0 0 1	
		IN 92-104	2	9 14 13	
		IN 105-105	1	2 0 0	
		IN 105-105	2	11 10 20	
Spontaneous tumor pct: 6% in ctrl. - Total			-	3 0 1	
THYROID GLAND	(TH )	IN 79-91	1	0 0 1	0.272 0.084 0.094
TISSUE MISSING	(000 )	IN 79-91	2	12 12 8	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 0 1	
THYROID GLAND	(TH )	IN 79-91	1	2 0 1	0.382 0.325 0.330
C-CELL ADENOMA	(102 )	IN 79-91	2	10 12 8	
		IN 92-104	1	0 3 4	
		IN 92-104	2	9 11 10	
		IN 105-105	1	4 2 5	
		IN 105-105	2	9 8 15	
Spontaneous tumor pct: 12% in ctrl. - Total			-	6 5 10	
THYROID GLAND	(TH )	IN 105-105	1	1 0 0	1.000 0.911 0.920
C-CELL CARCINOMA	(254 )	IN 105-105	2	12 10 20	
Spontaneous tumor pct: 2% in ctrl. - Total			-	1 0 0	
THYROID GLAND	(TH )	IN 53-78	1	1 1 0	0.749 0.666 0.675
FOLLIC: ADENOMA	(265 )	IN 53-78	2	12 7 6	
		IN 79-91	1	0 1 0	
		IN 79-91	2	12 11 9	
		IN 92-104	1	0 1 0	
		IN 92-104	2	9 13 14	
		IN 105-105	1	1 0 1	
		IN 105-105	2	12 10 19	
Spontaneous tumor pct: 4% in ctrl. - Total			-	2 3 1	
THYROID GLAND	(TH )	IN 53-78	1	1 0 0	0.809 0.721 0.731
FOLLIC C: CARCINOMA	(300 )	IN 53-78	2	12 8 6	
		IN 79-91	1	1 0 0	
		IN 79-91	2	11 12 9	
		IN 92-104	1	0 1 0	
		IN 92-104	2	9 13 14	
		IN 105-105	1	0 0 1	
		IN 105-105	2	13 10 19	
Spontaneous tumor pct: 4% in ctrl. - Total			-	2 1 1	

Table 4 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
THYMUS	(TM	) IN 0-52	1	0 2 0	0.042 0.032 0.033
TISSUE MISSING	(000	) IN 0-52	2	5 2 0	
		IN 53-78	1	2 3 2	
		IN 53-78	2	9 2 2	
		IN 79-91	1	3 3 3	
		IN 79-91	2	6 6 4	
		IN 92-104	1	2 5 6	
		IN 92-104	2	5 4 2	
		IN 105-105	1	6 0 8	
		IN 105-105	2	1 10 4	
Spontaneous tumor pct: 25%		in ctrl. - Total	-	13 13 19	
TONGUE	(TO	) IN 105-105	1	0 0 1	0.452 0.159 0.174
TISSUE MISSING	(000	) IN 105-105	2	13 10 18	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 0 1	
URINARY BLADDER	(UB	) IN 79-91	1	0 0 1	0.272 0.084 0.094
TISSUE MISSING	(000	) IN 79-91	2	12 12 8	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 0 1	
URETER	(UR	) IN 53-78	1	1 0 0	1.000 0.832 0.847
TISSUE MISSING	(000	) IN 53-78	2	11 8 6	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	1 0 0	

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Figure 3





1 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

Table 5

Number of Animals  
Species: Rat  
Sex: Female

Week	Treatment Group				
	CTRL1	CTRL2	MED	HIGH	Total
	N	N	N	N	N
0-52		2	1	1	5
53-78		9	6	11	45
79-91		13	11	10	44
92-104		12	8	15	41
105-105		15	24	13	66
Total		51	50	50	201

Table 6

Analysis of Mortality  
Species: Rat  
Sex: Female

Week	Dose											
	CTRL1			CTRL2			MED			HIGH		
	Num. of Dead	Num. at Risk	Cumu Pct. Died	Num. of Dead	Num. at Risk	Cumu Pct. Died	Num. of Dead	Num. at Risk	Cumu Pct. Died	Num. of Dead	Num. at Risk	Cumu Pct. Died
0-52	2	51	3.9	1	50	2.0	1	50	2.0	1	50	2.0
53-78	9	49	21.6	6	49	14.0	11	49	24.0	19	49	40.0
79-91	13	40	47.1	11	43	36.0	10	38	44.0	10	30	60.0
92-104	12	27	70.6	8	32	52.0	15	28	74.0	6	20	72.0
105-105	15	51	29.4	24	50	48.0	13	50	26.0	14	50	28.0

Table 7

Dose-Mortality Trend Tests

This test is run using Trend and Homogeneity Analyses of Proportions and Life Table Data Version 2.1, by Donald G. Thomas, National Cancer Institute

Species: Rat

Sex: Female

Method	Time-Adjusted Trend Test	Statistic	P Value
Cox	Dose-Mortality Trend	4.73	0.0296
	Depart from Trend	2.97	0.2268
	Homogeneity	7.70	0.0527
Kruskal-Wallis	Dose-Mortality Trend	6.91	0.0086
	Depart from Trend	2.45	0.2932
	Homogeneity	9.36	0.0248

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Table 8

Analysis of Carcinogenic Potential in Female Rat  
 Test of Dose-Response (Tumor) Positive Linear Trend  
 Study No. STUDY4412

Source:  

Note: Dose Levels Included: CTRL1 CTRL2 MED HIGH (0 0 10 20)  
 Missing value in Tumor-Caused Death is treated as tumor not causing death  
 Tumor Type: IN: Incidental (nonfatal) tumor, FA: Fatal tumor.

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
ADRENAL GLANDS	(AD )	IN 53-78	1	0 0 0 1	0.409 0.140 0.153
TISSUE MISSING	(000 )	IN 53-78	2	9 6 11 17	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 0 0 1	
ADRENAL GLANDS	(AD )	IN 105-105	1	1 0 0 1	0.418 0.253 0.267
U/ MED: MALIGNANT NEO	(141 )	IN 105-105	2	14 24 13 13	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1 0 0 1	
ADRENAL GLANDS	(AD )	IN 53-78	1	1 0 0 1	0.957 0.919 0.922
U/ MED: BENIGN NEO	(142 )	IN 53-78	2	8 6 11 17	
		IN 79-91	1	0 2 0 0	
		IN 79-91	2	13 9 10 10	
		IN 92-104	1	0 1 0 0	
		IN 92-104	2	12 7 15 6	
		IN 105-105	1	0 1 0 0	
		IN 105-105	2	15 23 13 14	
Spontaneous tumor pct: 5% in ctrl. - Total			-	1 4 0 1	
ADRENAL GLANDS	(AD )	IN 105-105	1	0 1 0 1	0.418 0.253 0.267
U/ CTX: CARCINOMA	(188 )	IN 105-105	2	15 23 13 13	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 1 0 1	
ADRENAL GLANDS	(AD )	IN 105-105	1	1 0 0 0	1.000 0.777 0.795
B/ MED: BENIGN NEOPLASM	(274 )	IN 105-105	2	14 24 13 14	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1 0 0 0	
ADRENAL GLANDS	(AD )	IN 92-104	1	0 1 0 2	0.110 0.047 0.052
U/ CTX: ADENOMA	(395 )	IN 92-104	2	12 7 15 4	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 1 0 2	
ADIPOSE TISSUE	(AT )	IN 92-104	1	1 0 0 0	1.000 0.825 0.842
TISSUE MISSING	(000 )	IN 92-104	2	10 8 15 6	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1 0 0 0	
FEMORAL MARROW	(BM2 )	IN 79-91	1	0 0 1 0	0.441 0.347 0.369
TISSUE MISSING	(000 )	IN 79-91	2	13 11 8 10	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 0 1 0	
BRAIN	(BN )	FA 104	1	0 1 0 0	1.000 0.772 0.790
GRANULAR C-TUMOR	(589 )	FA 104	2	15 25 13 14	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 1 0 0	

Table 8 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2x2 CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
FEMUR	(B02	) IN 79-91	1	0 0 1 0	0.441 0.347 0.369
TISSUE MISSING	(000	) IN 79-91	2	13 11 8 10	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 0 1 0	
CECUM	(CE	) IN 53-78	1	0 0 0 2	0.430 0.335 0.345
TISSUE MISSING	(000	) IN 53-78	2	9 6 11 15	
		IN 79-91	1	2 0 1 0	
		IN 79-91	2	9 11 8 10	
Spontaneous tumor pct: 2% in ctrl. - Total			-	2 0 1 2	
COLON	(CO	) IN 53-78	1	0 0 0 1	0.591 0.409 0.427
TISSUE MISSING	(000	) IN 53-78	2	9 6 11 17	
		IN 92-104	1	0 1 0 0	
		IN 92-104	2	12 6 15 6	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 1 0 1	
DUODENUM	(DU	) IN 53-78	1	0 1 0 1	0.842 0.781 0.788
TISSUE MISSING	(000	) IN 53-78	2	9 4 11 17	
		IN 79-91	1	1 1 1 0	
		IN 79-91	2	11 9 8 10	
		IN 92-104	1	1 0 1 0	
		IN 92-104	2	10 8 13 6	
Spontaneous tumor pct: 4% in ctrl. - Total			-	2 2 2 1	
EYES	(EY	) IN 53-78	1	0 0 0 1	0.217 0.134 0.143
TISSUE MISSING	(000	) IN 53-78	2	9 6 11 17	
		IN 105-105	1	0 0 1 0	
		IN 105-105	2	15 24 11 14	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 0 1 1	
ILEUM	(IL	) IN 53-78	1	0 1 0 2	0.346 0.287 0.293
TISSUE MISSING	(000	) IN 53-78	2	9 4 11 15	
		IN 79-91	1	5 2 2 3	
		IN 79-91	2	3 7 6 4	
		IN 92-104	1	1 0 1 1	
		IN 92-104	2	10 8 13 4	
Spontaneous tumor pct: 9% in ctrl. - Total			-	6 3 3 6	
JEJUNUM	(JE	) IN 0-52	1	1 0 0 0	0.632 0.581 0.586
TISSUE MISSING	(000	) IN 0-52	2	0 1 1 1	
		IN 53-78	1	3 3 3 7	
		IN 53-78	2	3 0 5 5	
		IN 79-91	1	7 3 4 4	
		IN 79-91	2	-1 5 2 2	
		IN 92-104	1	2 4 5 2	
		IN 92-104	2	8 0 5 2	
Spontaneous tumor pct: 23% in ctrl. - Total			-	13 10 12 13	
KIDNEYS	(KD	) IN 105-105	1	0 0 0 1	0.212 0.044 0.050
U/ LIPOMATOUS NEOPLASM	(626	) IN 105-105	2	15 24 13 13	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 0 0 1	

Table 8 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
MESENTERIC LN	(L1	) IN 53-78	1	0 0 0 1	0.856 0.792 0.799
TISSUE MISSING	(000	) IN 53-78	2	9 6 11 17	
		IN 79-91	1	1 1 1 0	
		IN 79-91	2	11 9 8 10	
		IN 92-104	1	1 1 0 0	
		IN 92-104	2	10 6 15 6	
Spontaneous tumor pct: 4%		in ctrl. - Total	-	2 2 1 1	
MESENTERIC LN	(L1	) IN 105-105	1	0 1 0 0	1.000 0.777 0.795
HEMANGIOSARCOMA	(682	) IN 105-105	2	15 23 13 14	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 1 0 0	
MEDIASTINAL LN	(L2	) IN 0-52	1	0 0 1 0	0.436 0.374 0.381
TISSUE MISSING	(000	) IN 0-52	2	2 1 -1 1	
		IN 53-78	1	0 1 0 1	
		IN 53-78	2	9 4 11 17	
		IN 79-91	1	0 0 3 2	
		IN 79-91	2	13 11 4 6	
		IN 92-104	1	3 2 0 0	
		IN 92-104	2	6 4 15 6	
		IN 105-105	1	0 0 1 0	
		IN 105-105	2	15 24 11 14	
Spontaneous tumor pct: 6%		in ctrl. - Total	-	3 3 5 3	
SUBMANDIB/MAX LN	(L4	) IN 53-78	1	0 1 0 0	0.446 0.307 0.321
TISSUE MISSING	(000	) IN 53-78	2	9 4 11 19	
		IN 92-104	1	0 0 1 1	
		IN 92-104	2	12 8 13 4	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 1 1 1	
LACRIMAL GLANDS	(LG	) IN 53-78	1	1 1 0 1	0.855 0.805 0.810
TISSUE MISSING	(000	) IN 53-78	2	7 4 11 17	
		IN 79-91	1	1 2 2 1	
		IN 79-91	2	11 7 6 8	
		IN 92-104	1	1 0 0 0	
		IN 92-104	2	10 8 15 6	
Spontaneous tumor pct: 6%		in ctrl. - Total	-	3 3 2 2	
LIVER	(LI	) IN 105-105	1	0 1 0 0	1.000 0.777 0.795
HEPATO: CARCINOMA	(260	) IN 105-105	2	15 23 13 14	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 1 0 0	
LIVER	(LI	) IN 105-105	1	0 1 0 0	1.000 0.777 0.795
HEPATOCELLULAR ADENOMA	(672	) IN 105-105	2	15 23 13 14	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 1 0 0	

Table 8 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2x2 CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
LYMPH/RETIC TIS	(LR	) IN 53-78	1	0 1 0 0	0.895 0.834 0.842
HISTIOCYTIC SARCOMA	(221	) IN 53-78	2	9 5 11 19	
		FA 100	1	0 1 0 0	
		FA 100	2	23 26 20 18	
		FA 101	1	0 0 1 0	
		FA 101	2	20 26 18 18	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	0 2 1 0	
LYMPH/RETIC TIS	(LR	) IN 53-78	1	1 0 0 0	0.816 0.733 0.747
MYELOSARC/GRAN-LEUK	(315	) IN 53-78	2	8 6 11 19	
		FA 92	1	0 0 1 0	
		FA 92	2	27 32 27 20	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	1 0 1 0	
LYMPH/RETIC TIS	(LR	) IN 92-104	1	1 0 0 0	1.000 0.820 0.837
THYMIC LYMPHOMA	(518	) IN 92-104	2	11 8 15 6	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	1 0 0 0	
LYMPH/RETIC TIS	(LR	) IN 105-105	1	0 1 0 0	1.000 0.777 0.795
MONONUCLEAR C-LEUKEMIA	(738	) IN 105-105	2	15 23 13 14	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 1 0 0	
LUNGS	(LU	) IN 53-78	1	0 0 1 0	0.666 0.540 0.563
BRNCH-ALVEO CARCINOMA	(281	) IN 53-78	2	9 6 10 19	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 0 1 0	
LUNGS	(LU	) IN 105-105	1	0 0 0 2	0.042 0.007 0.008
BRONCHO/ALVEOLAR ADENOMA	(371	) IN 105-105	2	15 24 13 12	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 0 0 2	
					(Exact P<0.050)
MAMMARY	(MG	) IN 53-78	1	0 0 0 1	0.586 0.399 0.416
TISSUE MISSING	(000	) IN 53-78	2	9 6 11 17	
		IN 105-105	1	1 0 0 0	
		IN 105-105	2	13 24 13 14	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	1 0 0 1	
MAMMARY	(MG	) IN 53-78	1	2 2 3 5	0.447 0.412 0.415
CARCINOMA	(055	) IN 53-78	2	7 4 8 13	
		IN 79-91	1	5 2 1 3	
		IN 79-91	2	7 9 9 7	
		IN 92-104	1	4 1 5 0	
		IN 92-104	2	8 7 10 6	
		IN 105-105	1	3 9 5 7	
		IN 105-105	2	11 15 8 7	
		FA 88	1	1 0 0 0	
		FA 88	2	30 37 29 23	
Spontaneous tumor pct: 29%		in ctrl. - Total	-	15 14 14 15	

Table 8 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2x2 CONTINGENCY -----TABLES-----				EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
MAMMARY FIBROADENOMA	(MG 082)	) IN 0-52	1	1	0	0	0	0.081 0.069 0.070
		) IN 0-52	2	1	1	1	1	
		IN 53-78	1	1	2	2	9	
		IN 53-78	2	8	4	9	9	
		IN 79-91	1	6	4	6	6	
		IN 79-91	2	7	7	4	4	
		IN 92-104	1	6	5	11	5	
		IN 92-104	2	6	3	4	1	
		IN 105-105	1	8	19	6	9	
		IN 105-105	2	6	5	7	5	
Spontaneous tumor pct: 51% in ctrl. - Total				-	22	30	25 29	
MAMMARY CARCINO-SARCOMA	(MG 473)	) FA 85	1	1	0	0	0	1.000 0.869 0.878
		) FA 85	2	34	39	34	25	
		FA 102	1	1	0	0	0	
		FA 102	2	17	26	16	16	
Spontaneous tumor pct: 2% in ctrl. - Total				-	2	0	0 0	
MAMMARY ADENOMA	(MG 483)	) IN 53-78	1	0	1	1	0	0.889 0.818 0.826
		) IN 53-78	2	9	5	10	18	
		IN 79-91	1	0	0	1	0	
		IN 79-91	2	13	11	9	10	
		IN 92-104	1	1	0	0	0	
		IN 92-104	2	11	8	15	6	
Spontaneous tumor pct: 2% in ctrl. - Total				-	1	1	2 0	
MAMMARY MALIGNANT MIXED TUMOR	(MG 638)	) IN 105-105	1	0	0	1	0	0.415 0.325 0.347
		) IN 105-105	2	14	24	12	14	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	1 0	
OPTIC NERVE TISSUE MISSING	(ON 000)	) IN 53-78	1	0	1	0	0	0.970 0.935 0.938
		) IN 53-78	2	9	4	11	19	
		IN 92-104	1	4	0	0	1	
		IN 92-104	2	4	8	15	4	
Spontaneous tumor pct: 5% in ctrl. - Total				-	4	1	0 1	
OVARIES TISSUE MISSING	(OV 000)	) IN 53-78	1	1	0	0	0	1.000 0.902 0.912
		) IN 53-78	2	7	6	11	19	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0 0	
OVARIES SERTOLIFORM CELL TUMOR	(OV 430)	) IN 105-105	1	1	0	0	1	0.418 0.253 0.267
		) IN 105-105	2	14	24	13	13	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0 1	
OVARIES U/ LEUTEOMA	(OV 653)	) IN 105-105	1	0	1	0	0	1.000 0.777 0.795
		) IN 105-105	2	15	23	13	14	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0 0	



Table 8 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2x2 CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
OVARIES	(OV	) IN 92-104	1	0 1 0 0	1.000 0.820 0.837
U/ FIBROSARCOMA	(670	) IN 92-104	2	12 7 15 6	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 1 0 0	
PANCREAS	(PA	) IN 53-78	1	0 0 0 1	0.743 0.624 0.637
TISSUE MISSING	(000	) IN 53-78	2	9 6 11 17	
		IN 79-91	1	1 0 0 0	
		IN 79-91	2	11 11 10 10	
		IN 92-104	1	0 1 0 0	
		IN 92-104	2	12 6 15 6	
Spontaneous tumor pct: 2% in ctrl. - Total			-	1 1 0 1	
PANCREAS	(PA	) IN 79-91	1	1 0 0 0	1.000 0.944 0.947
ISLET C: ADENOMA	(384	) IN 79-91	2	11 11 10 10	
		IN 105-105	1	1 2 0 0	
		IN 105-105	2	14 22 13 14	
Spontaneous tumor pct: 4% in ctrl. - Total			-	2 2 0 0	
PANCREAS	(PA	) IN 105-105	1	1 0 0 0	1.000 0.777 0.795
ACINAR C: ADENOMA	(432	) IN 105-105	2	14 24 13 14	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1 0 0 0	
PANCREAS	(PA	) FA 100	1	1 0 0 0	1.000 0.786 0.804
ACINAR C: CARCINOMA	(486	) FA 100	2	22 27 20 18	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1 0 0 0	
PANCREAS	(PA	) IN 92-104	1	1 0 0 0	1.000 0.825 0.842
ISLET CELL CARCINOMA	(741	) IN 92-104	2	11 7 15 6	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1 0 0 0	
PREPUT/CLIT GL	(PC	) IN 79-91	1	0 1 0 0	1.000 0.797 0.814
ADENOMA	(665	) IN 79-91	2	13 10 10 10	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 1 0 0	
PITUITARY GLAND	(PG	) IN 53-78	1	0 1 0 1	0.899 0.831 0.839
TISSUE MISSING	(000	) IN 53-78	2	9 4 11 17	
		IN 79-91	1	1 0 0 0	
		IN 79-91	2	11 11 10 10	
		IN 92-104	1	0 1 0 0	
		IN 92-104	2	12 6 15 6	
Spontaneous tumor pct: 3% in ctrl. - Total			-	1 2 0 1	

Table 8 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB			
					PROB	PROB	/CONT	CORR
					=P(STAT .GE. OBSERVED)			
PITUITARY GLAND	(PG	) IN 53-78	1	0 0 2 6	0.091 0.080 0.081			
P-DIST: ADENOMA	(083	) IN 53-78	2	2 0 2 5				
		IN 79-91	1	4 1 3 3				
		IN 79-91	2	1 1 2 1				
		IN 92-104	1	1 0 6 2				
		IN 92-104	2	2 5 3 0				
		IN 105-105	1	11 17 10 12				
		IN 105-105	2	4 7 3 2				
		FA 46	1	0 0 1 0				
		FA 46	2	49 48 49 48				
		FA 47	1	0 1 0 0				
		FA 47	2	48 47 49 48				
		FA 58	1	0 0 1 0				
		FA 58	2	48 47 48 48				
		FA 62	1	0 0 1 0				
		FA 62	2	47 47 46 47				
		FA 66	1	0 0 1 1				
		FA 66	2	47 47 44 45				
		FA 67	1	1 0 0 2				
		FA 67	2	45 47 44 43				
		FA 69	1	1 0 0 1				
		FA 69	2	44 47 43 39				
		FA 72	1	0 1 1 0				
		FA 72	2	44 46 42 39				
		FA 73	1	2 0 0 1				
		FA 73	2	42 46 42 38				
		FA 74	1	0 0 0 1				
		FA 74	2	42 46 42 36				
		FA 75	1	0 1 2 1				
		FA 75	2	42 45 40 34				
		FA 76	1	2 0 0 0				
		FA 76	2	40 45 40 34				
		FA 77	1	1 2 1 0				
		FA 77	2	39 43 39 33				
		FA 78	1	0 1 0 0				
		FA 78	2	39 42 39 30				
		FA 80	1	0 0 1 0				
		FA 80	2	39 41 37 30				
		FA 81	1	1 0 1 2				
		FA 81	2	38 41 35 28				
		FA 83	1	1 1 0 2				
		FA 83	2	37 40 35 25				
		FA 84	1	1 2 0 0				
		FA 84	2	36 38 35 25				
		FA 85	1	0 0 0 1				
		FA 85	2	35 38 34 24				
		FA 86	1	2 2 2 0				
		FA 86	2	32 36 32 24				
		FA 87	1	1 0 1 0				
		FA 87	2	31 36 29 23				
		FA 88	1	0 2 0 0				

Table 8 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY				EXACT ASYMP ASYMP PROB			
				-----TABLES-----				PROB	PROB	/CONT	CORR
								=P(STAT .GE. OBSERVED)			
		FA 88	2	31	34	29	23				
		FA 90	1	1	1	0	1				
		FA 90	2	28	32	28	21				
		FA 91	1	0	1	0	0				
		FA 91	2	28	31	28	20				
		FA 92	1	1	0	0	0				
		FA 92	2	26	31	28	20				
		FA 93	1	1	1	1	0				
		FA 93	2	25	30	26	20				
		FA 94	1	1	1	0	0				
		FA 94	2	24	28	26	20				
		FA 95	1	0	0	1	0				
		FA 95	2	24	28	25	20				
		FA 96	1	0	0	2	1				
		FA 96	2	24	28	23	19				
		FA 97	1	0	0	0	1				
		FA 97	2	24	27	22	18				
		FA 98	1	1	0	0	0				
		FA 98	2	23	27	22	18				
		FA 99	1	0	0	1	0				
		FA 99	2	23	26	20	18				
		FA 100	1	1	0	0	0				
		FA 100	2	22	26	20	18				
		FA 101	1	1	0	0	1				
		FA 101	2	19	26	19	17				
		FA 102	1	3	0	0	0				
		FA 102	2	16	26	16	16				
		FA 103	1	0	0	1	1				
		FA 103	2	15	26	13	15				
Spontaneous tumor pct: 73%		in ctrl. - Total	-	39	35	40	40				
PITUITARY GLAND	(PG	) IN 105-105	1	0	2	0	0	0.419	0.329	0.339	
P-DIST: CARCINOMA	(581	) IN 105-105	2	15	22	13	14				
		FA 73	1	0	0	0	1				
		FA 73	2	44	46	42	38				
		FA 89	1	0	0	1	0				
		FA 89	2	29	34	28	22				
		FA 102	1	0	0	1	0				
		FA 102	2	19	26	15	16				
Spontaneous tumor pct: 2%		in ctrl. - Total	-	0	2	2	1				
PARATHYROID GLS.	(PT	) IN 0-52	1	0	1	0	0	0.908	0.881	0.884	

Table 8 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2x2 CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
TISSUE MISSING	(000	) IN 0-52	2	2 -1 1 1	
		IN 53-78	1	2 0 1 2	
		IN 53-78	2	5 6 9 15	
		IN 79-91	1	0 1 1 1	
		IN 79-91	2	13 9 8 8	
		IN 92-104	1	2 0 1 1	
		IN 92-104	2	8 8 13 4	
		IN 105-105	1	2 5 1 0	
		IN 105-105	2	11 14 11 14	
Spontaneous tumor pct: 13%		in ctrl. - Total	-	6 7 4 4	
PARATHYROID GLS.	(PT	) IN 92-104	1	0 1 0 0	1.000 0.821 0.838
ADENOMA	(554	) IN 92-104	2	10 7 14 5	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 1 0 0	
LOW COLON/RECTUM	(RC	) IN 53-78	1	0 0 0 1	0.591 0.409 0.427
TISSUE MISSING	(000	) IN 53-78	2	9 6 11 17	
		IN 92-104	1	0 1 0 0	
		IN 92-104	2	12 6 15 6	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 1 0 1	
CERVICAL SC	(SC1	) IN 79-91	1	0 2 0 0	1.000 0.892 0.900
TISSUE MISSING	(000	) IN 79-91	2	13 7 10 10	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	0 2 0 0	
SALIVARY GLANDS	(SG	) IN 79-91	1	0 0 1 0	0.673 0.603 0.620
TISSUE MISSING	(000	) IN 79-91	2	13 11 8 10	
		IN 105-105	1	0 1 0 0	
		IN 105-105	2	15 22 13 14	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 1 1 0	
SKIN	(SK	) IN 105-105	1	1 0 0 0	1.000 0.780 0.798
TISSUE MISSING	(000	) IN 105-105	2	13 24 13 14	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	1 0 0 0	
SKIN	(SK	) IN 53-78	1	0 1 1 0	0.932 0.881 0.886
FIBROSARCOMA	(381	) IN 53-78	2	9 5 10 19	
		IN 79-91	1	2 0 0 0	
		IN 79-91	2	11 11 10 10	
		FA 98	1	0 0 1 0	
		FA 98	2	23 28 21 18	
Spontaneous tumor pct: 3%		in ctrl. - Total	-	2 1 2 0	
SKIN	(SK	) IN 53-78	1	0 0 0 1	0.372 0.268 0.278
FIBROMA	(385	) IN 53-78	2	9 6 11 18	
		IN 92-104	1	0 0 1 0	
		IN 92-104	2	12 8 14 6	
		IN 105-105	1	0 1 1 0	
		IN 105-105	2	14 23 12 14	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 1 2 1	

Table 8 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
SKIN	(SK	) IN 105-105	1	0 1 0 0	1.000 0.780 0.798
LIPOSARCOMA	(669	) IN 105-105	2	14 23 13 14	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 1 0 0	
IMPLANT ST-COMB	(SK3	) IN 53-78	1	0 0 1 4	0.495 0.446 0.451
ZT: CAPSULE-IMPLANT SITE	(050	) IN 53-78	2	9 6 9 11	
		IN 79-91	1	2 1 0 1	
		IN 79-91	2	9 9 10 8	
		IN 92-104	1	1 0 0 0	
		IN 92-104	2	10 8 15 6	
		IN 105-105	1	3 8 8 2	
		IN 105-105	2	9 8 3 10	
Spontaneous tumor pct: 15% in ctrl. - Total			-	6 9 9 7	
IMPLANT ST-COMB	(SK3	) IN 92-104	1	0 1 0 0	0.849 0.762 0.774
FIBROSARCOMA	(650	) IN 92-104	2	11 7 15 6	
		FA 84	1	0 0 1 0	
		FA 84	2	32 32 26 22	
		FA 89	1	0 1 0 0	
		FA 89	2	25 26 21 20	
Spontaneous tumor pct: 2% in ctrl. - Total			-	0 2 1 0	
STOMACH	(ST	) IN 53-78	1	0 0 0 1	0.242 0.127 0.137
TISSUE MISSING	(000	) IN 53-78	2	9 6 11 17	
		IN 92-104	1	0 0 1 0	
		IN 92-104	2	12 8 13 6	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 0 1 1	
THYROID GLAND	(TH	) IN 53-78	1	0 0 0 1	0.085 0.026 0.029
TISSUE MISSING	(000	) IN 53-78	2	9 6 11 17	
		IN 79-91	1	0 0 0 1	
		IN 79-91	2	13 11 10 8	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 0 0 2	
THYROID GLAND	(TH	) IN 53-78	1	0 0 2 1	0.059 0.039 0.041
C-CELL ADENOMA	(102	) IN 53-78	2	9 6 9 17	
		IN 79-91	1	1 0 1 0	
		IN 79-91	2	12 11 9 9	
		IN 105-105	1	2 1 3 4	
		IN 105-105	2	13 23 10 10	
Spontaneous tumor pct: 4% in ctrl. - Total			-	3 1 6 5	
THYROID GLAND	(TH	) IN 105-105	1	0 1 1 0	0.654 0.584 0.601
C-CELL CARCINOMA	(254	) IN 105-105	2	15 23 12 14	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0 1 1 0	
THYROID GLAND	(TH	) IN 92-104	1	0 0 1 0	0.589 0.470 0.485
FOLLIC: ADENOMA	(265	) IN 92-104	2	12 8 14 6	
		IN 105-105	1	1 0 1 0	
		IN 105-105	2	14 24 12 14	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1 0 2 0	

Table 8 (continued)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
THYMUS	(TM	) IN 0-52	1	0 1 0 0	0.564 0.521 0.525
TISSUE MISSING	(000	) IN 0-52	2	2 -1 1 1	
		IN 53-78	1	1 2 3 6	
		IN 53-78	2	7 2 5 7	
		IN 79-91	1	4 3 5 4	
		IN 79-91	2	5 5 0 2	
		IN 92-104	1	7 2 4 2	
		IN 92-104	2	-2 4 7 2	
		IN 105-105	1	1 6 0 1	
		IN 105-105	2	13 12 13 12	
Spontaneous tumor pct: 27% in ctrl. - Total				- 13 14 12 13	
TRACHEA	(TR	) IN 92-104	1	0 0 1 0	0.512 0.317 0.342
SARCOMA (NOS)	(742	) IN 92-104	2	12 8 14 6	
Spontaneous tumor pct: <= 1% in ctrl. - Total				- 0 0 1 0	
URINARY BLADDER	(UB	) IN 53-78	1	0 0 0 2	0.326 0.203 0.213
TISSUE MISSING	(000	) IN 53-78	2	9 6 11 15	
		IN 79-91	1	1 0 0 0	
		IN 79-91	2	11 11 10 10	
Spontaneous tumor pct: <= 1% in ctrl. - Total				- 1 0 0 2	
URETER	(UR	) IN 0-52	1	1 0 0 0	1.000 0.817 0.832
TISSUE MISSING	(000	) IN 0-52	2	0 1 1 1	
Spontaneous tumor pct: <= 1% in ctrl. - Total				- 1 0 0 0	
UTERUS	(UT	) IN 79-91	1	1 0 0 0	1.000 0.797 0.814
ENDOMET: CARCINOMA	(469	) IN 79-91	2	12 11 10 10	
Spontaneous tumor pct: <= 1% in ctrl. - Total				- 1 0 0 0	
UTERUS	(UT	) IN 105-105	1	0 2 0 0	1.000 0.862 0.871
ENDOMETRIAL STROMAL POLYP	(661	) IN 105-105	2	15 22 13 14	
Spontaneous tumor pct: 2% in ctrl. - Total				- 0 2 0 0	
VAGINA	(VA	) IN 53-78	1	1 1 0 1	0.943 0.896 0.902
TISSUE MISSING	(000	) IN 53-78	2	7 4 11 17	
		IN 92-104	1	1 0 0 0	
		IN 92-104	2	10 8 15 6	
Spontaneous tumor pct: 3% in ctrl. - Total				- 2 1 0 1	